

Atomic Resolution Structures of the Core Domain of Avian Sarcoma Virus Integrase and its D64N Mutant

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Six crystal structures of the core domain of integrase (IN) from avian sarcoma virus (ASV) and its active-site derivative containing an Asp64 --> Asn substitution have been solved at atomic resolution ranging 1.02-1.42 Å. The high-quality data provide new structural information about the active site of the enzyme and clarify previous inconsistencies in the description of this fragment. The very high resolution of the data and excellent quality of the refined models explain the dynamic properties of IN and the multiple conformations of its disordered residues. They also allow an accurate description of the solvent structure and help to locate other molecules bound to the enzyme. A detailed analysis of the flexible active-site region, in particular the loop formed by residues 144-154, suggests conformational changes which may be associated with substrate binding and enzymatic activity. The pH-dependent conformational changes of the active site loop correlates with the pH vs activity profile observed for ASV IN.